

### **REMARKS**

The rejection of claims on grounds of double patenting and lack of sufficient written description have been withdrawn. Claims 1-11, 13-18, 21-23, 27-92 and 56-57 have been examined and stand rejected.

Claims 1-4, 7-11, 13-18, 21-23, 42-43, and 46-52 are rejected as obvious over Pirrung et al. (U.S. Patent No. 5,143,854, hereinafter "Pirrung") in view of Derndinger et al. (U.S. Patent No. 5,239,178 (hereinafter "Derndinger")). It is the Office's position that Pirrung discloses a substrate with a plurality of polymer sequences in predefined regions, made using linkers with photoremoveable protective groups. In particular, the Office Action refers to the apparatus for preparing the substrate as comprising a light source and a mask. See Office Action, page 5, lines 1. The method of synthesis in Pirrung is described as exposing the surface to light using a mask to direct light to selected regions of the surface during synthetic steps to produce an array of different polymers. The method disclosed in this application does not use mask technology at all. Light is directed to specific areas on the substrate surface by a light matrix, not a light source and a mask. Furthermore, the position of the illumination on the surface is detected using a light sensor matrix to confirm the correct location of illumination (the illumination pattern) and allow it to be adjusted if necessary to ensure the correct locations are being illuminated. See the specification as a whole and step (c) of claim 1.

In Pirrung, the chip manufacture and detection steps described there are completely separate devices—one to make the chip and another to detect fluorescence after the chip is made and used for an assay. Pirrung does not disclose a light sensor matrix in the physical arrangement of the claim or any manner of detecting where the illumination pattern from the light source (or light sensor matrix) is placed. The discussion of Pirrung in the Action completely ignores step (c) of claim 1 here.

Pirrung does not discuss, mention, or even hint at a system that comprises a light sensor matrix or any methodology capable of detecting the light

impinging on the substrate surface during synthesis to detect the illumination location on the surface. The only light sensing even mentioned in Pirrung is the detection of binding to an already-completed array when it is being used in an assay. This is a detection of fluorescent light signals emanating from the bound ligand on the surface. Pirrung does not disclose or hint at step (c) of claim 1 and the Office Action completely ignores this recited step in attempting to make out its case of obviousness.

Applicant has amended claim 1 by rewriting as new claim 58 in an attempt to make clear the aspects of the invention discussed above. In particular, this new claim recites a method using a light-producing matrix and a light-detecting matrix in defined relationship where the biochip carrier is illuminated to produce a two-dimensional light exposure pattern which is detected by the detection matrix. Pirrung does not teach, suggest or refer to any method whatsoever that involves detection of illumination from its "light source." It only detects fluorescent label from material bound to the array after its synthesis already has been completed. Therefore, Pirrung cannot be said to guide the skilled reader to the apparatus of the present invention.

The Dermdinger reference is cited as teaching a device for examination of an object, which includes an illumination grid and a detector grid, with an arrangement that allows light to be focused on the object. The reference refers to computer-control of light sources or light dots with respect to each other in the direction of the optical axis and/or the plane of focus. Figure 8 depicts a device where the object being imaged is between the light source and the CCD receiver (detector). Although the Office Action states that the computer allows adjustment of the illumination grid and/or the object, Office Action, page 6, last two lines, the text cited refers only to adjusting the focal plane by moving the light source and object relative to each other and moving the object in planes perpendicular to the optical axis in order to scan the object.

The amendments to the claims here clarify the aspect of the invention here of concurrent quality control during biochip manufacture by confirming that

the illumination for photoactivation of specific zones is actually falling on the precise desired locations. This step is lacking in the art. Derndinger discloses a microscope device to examine an object in focal planes. It discloses a detector grid to image the object which can be adjusted, but it does not disclose or even hint at a method of adjusting the illumination pattern. It only relates to movement of the light and detector closer or further away from each other to focus an image as light scans the object back and forth. See col. 4, lines 14-17. There is not suggestion or hint that the pattern of illumination, i.e. the locations of light impingement on the surface, could be detected or adjusted here because there is no illumination pattern in Derndinger at all. There is no mention in Derndinger at all concerning confirming the correctness of the location of illumination on the object being imaged, since the process requires a scanning of the entire object by moving the object across the plane being imaged relative to the camera and also adjusting the focus to obtain a good image.

The art of Derndinger does not even relate to producing an illumination pattern or any aspect of biochip manufacture. Further, it does not relate to methods for specifically producing a two-dimensional light pattern and does not contain any system whereby such a two-dimensional pattern could be detected in terms of location. The detection of Derndinger only relates to capturing an image and does not hint that the location of light pixels shown onto the object being imaged could be detected, or even that such a type of detection could be useful for any purpose. The Derndinger detector only records an image for viewing, it does not detect the location of illumination as recited in the claims here.

The Office urges that the Pirrung and Derndinger references would be combined, even though they relate to two disparate arts and to two different problems which would not be considered by a skilled person to be analogous. The problem that the current invention solves is to more accurately synthesize biochip arrays by being able to confirm and adjust where the light is falling on the surface during synthesis. In this way, the location where addition of the array's

building blocks are attached is more accurate and, if necessary, can be adjusted when light is not illuminating the exactly correct locations.

Pirrung does not detect where light illuminates the biochip through the mask and Dermdinger does not detect where light illuminates the object being imaged in two dimensions. The methods of Dermdinger would not assist the skilled person attempting to improve Pirrung because the artisans practicing Dermdinger do not care where in two dimensions the light pattern is precisely falling and do not have a method to determine it. Therefore a skilled artisan who wanted to improve the accuracy of light exposure location when employing the mask technology of Pirrung would not seek out Dermdinger.

Even if the Pirrung and Dermdinger references were combined, the Pirrung biochip manufacturing method would incorporate a method of imaging (photographing the biochip as it was being manufactured. There still would be no method which could detect the location of the two-dimensional light exposure pattern since Dermdinger's adjustments only allow one to focus an image or to move the area being imaged, not specifically illuminate only the precise desired pattern of illumination on a surface.

In summary, the Office considers previous arguments non-persuasive because the elements not taught in the prior art assertedly are not recited in the rejected claims. The Office Action, however, has completely ignored claim 1, step (c), which was recited in the previous claims. Applicants request the Office review the newly revised claims and focus on these elements.

The Office, its reply to Applicant's arguments, refers to "detecting a hybridization." See page 9, line 8. Pirrung uses a methodology for detecting hybridization, but the present claims do not – they clearly recite detecting the location of the illumination of the two-dimensional light exposure pattern, and not a hybridization event. The present independent claims do not encompass detecting signals produced by probes hybridized on a microarray. The Dermdinger system cannot detect the location of illumination on a two-dimensional surface and does not hint that such would be desirable. The Office

Action refers to col. 6, lines 9-11 of Derndinger, which states that the object can be moved in three dimensions so it can be scanned in different layers. This scanning does not refer to detecting the location of light pixels illuminating the object. It only refers to moving the object with respect to the light source to focus light on the entire object in sequence. There is no method in Derndinger which allows one to precisely determine the location of the elements of an illumination pattern on the object.

The Office also refers to Applicant's arguments "against the references individually." Applicant submits that the Office cited the references individually and discussed the disclosures of each reference, as would be required to make out its case, and then refers to the reasons for combining the references and the results of the combination. It is difficult to see an alternative method to make the arguments. Applicant also has followed this traditional format and submits that if neither art reference discloses or suggests a claim element, then the combination of such references also cannot teach or suggest that element absent some articulated reason why the combination of two references which each individually fail to disclose or even hint at any method to detect the location of an illumination pattern on a surface do so when combined.

Applicant requests that the Office reconsider the claims as amended in view of the arguments made herein and made in previous response. The claims now recite more clearly the features that the Office had asserted were not recited. Applicant requests withdrawal of this rejection.

Claims 27-41, 44 and 45, claims 56 and 57, and claims 5 and 6 are rejected as obvious over the same two references discussed and cited in the above rejection, and in the case of claims 5 and 6 further in view of Cerrina et al. No specific additional reasons for these separate rejections are provided, however the Office contends that the issues involved in the latter three rejections were addressed above.

Applicant repeats that no single reference cited against the claims here (individually) discusses, suggests or even hints at any method for detecting the

location of illumination of an illumination pattern or a surface or any apparatus which is capable of doing so. Furthermore, no reference provides any motivation for developing such a method or apparatus or even recognizes a problem that such a method or apparatus could solve. Therefore, there is no motivation to develop what is claimed here. Even when combined, none of the disclosures in any cited reference can make up for the complete failure to provide this claim element in the other references. Their combination is a method of imaging a biochip and detecting hybridization to it – not a method of detecting the position of illumination during synthesis.


Applicant therefore requests that the three rejections of claims 27-41, 44-45 and 56-57 as obvious be withdrawn.

Applicant refers the Office to the following recitations in the original specification for support for the amendments herein: page 14, lines 11-14, page 17, line 34 – page 18, line 4, page 20, lines 21-23, page 25, lines 1-3, page 33, lines 22-25, page 34, lines 1-3, page 35, lines 33-39, original claims 19, 20, 30 and 41, and the drawings, particularly Figures 1 and 7. New claim 58 is added to replace claim 1. Some claims have been canceled as redundant in view of this amendment. Other claims have been amended to improve readability and to ensure proper antecedent basis in view of the amendment to claim 58 (formerly claim 1).

Applicant requests reconsideration of the claims as amended and allowance of the application at this time.

Respectfully submitted,

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